A NOTE ON THE EFFECT OF NICOTINE INJECTION ON ADRENAL SECRETION

BY

W. B. CANNON, J. C. AUB, AND C. A. L. BINGER

From the Laboratory of Physiology in the Harvard Medical School

REPRINTED FROM
THE JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS
VOL. III, NO. 4. MARCH, 1912

C.

WELLCOME INSTITUTE
LIBRARY
Coll. WELLCOME
Coll.
No. WK 700
1912
C220

Reprinted from THE JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS
VOL. III, No. 4, March, 1912

A NOTE ON THE EFFECT OF NICOTINE INJECTION ON ADRENAL SECRETION

W. B. CANNON, J. C. AUB, AND C. A. L. BINGER

From the Laboratory of Physiology in the Harvard Medical School

Received for publication, January 27, 1912

The observations of Dreyer,[1] Tscheboksaroff,[2] and Asher[3] have proved that adrenal secretion is under the control of the thoracico-lumbar autonomic (sympathetic) system. Langley and Dickenson concluded from their studies of the action of nicotine that it at first stimulates and later paralyses sympathetic ganglia.[4] Small doses of nicotine might, therefore, be expected to cause an increase of adrenal secretion by stimulating the ganglia occurring in the sympathetic supply of the adrenal glands.

The present investigation was undertaken to learn whether nicotine can in fact increase the discharge of epinephrin into the blood. Cats, under complete ether anaesthesia, were used for the experiments. The method of testing for the presence of epinephrin was that devised by Cannon and de la Paz.[5] The longitudinal strips of intestinal smooth muscle were taken through a small abdominal incision from the animal later to be injected with nicotine. The strips were cut into convenient lengths and placed in aërated Ringer's solution kept at approximately 37° C.

The blood to be tested was removed, as in the experiments of Cannon and de la Paz, by introducing a fine catheter vaselined inside and out, through the left femoral vein into the inferior vena cava to a point immediately anterior to the opening of the adrenal

[1] Dreyer: Am. Jour. Physiol., 1898–99, ii, p. 219.
[2] Tscheboksaroff: Arch. f. d. ges. Physiol., 1910, cxxxvii, p. 103.
[3] Asher: Zentralbl. f. Physiol., 1910, xxiv, p. 927.
[4] Langley and Dickenson: Jour. Physiol., 1890, xi, p. 303.
[5] Cannon and de la Paz: Am. Jour. Physiol., 1911, xxviii, p. 65.

veins. To the catheter was attached a small glass aspirator by which the blood was withdrawn.

Before injection of the nicotine solution a sample of blood (to be called "blood A") was extracted. The time of extraction was noted. The blood was transferred immediately to a beaker, defibrinated by whipping, and then set in a water-bath at 37° C. A cannula was now inserted into the right femoral vein and the solution of nicotine (Merck's) was allowed to run in slowly. The time of this injection was taken. After an interval varying usually between three and five minutes blood was again extracted by means of the catheter, from the same region in the inferior vena cava; the blood was defibrinated as before, and preserved at body temperature. This was "blood B." In some of the experiments a third extraction ("blood C") was made ten to twelve minutes after the end of the nicotine injection.

The several specimens of blood—A, B and C—were then tested for their content of epinephrin. The strip of intestinal muscle, attached to a writing lever, was suspended between two *serres fines* in a small cylindrical chamber through which air was passed. The chamber was surrounded by water at 37° C. The characteristic inhibition of the rhythmic contractions of the muscle, even when it has been for some time removed from the body, occurs at a dilution of adrenalin 1:2,000,000 in defibrinated blood.[6]

In testing the samples of blood the first step consisted in securing a record of the rhythmic contractions of the intestinal strip when surrounded by warm aërated Ringer's solution. The solution was then withdrawn by means of a fine pipette, and blood A was substituted. After the muscle had come to a condition of constancy, blood A was withdrawn, and blood B (removed from the animal after the nicotine injection) was substituted. The muscle was again allowed to reach a constant condition, whereupon blood B was replaced by blood A or by Ringer's solution.

The results which were secured are illustrated in the accompanying tracings.

The animal whose blood-reaction is presented in Fig. 1 received 0.0037 gram (0.75 cc. of 1 : 200) of nicotine. The registering

[6] Cannon and de la Paz: Loc. cit., p. 69.

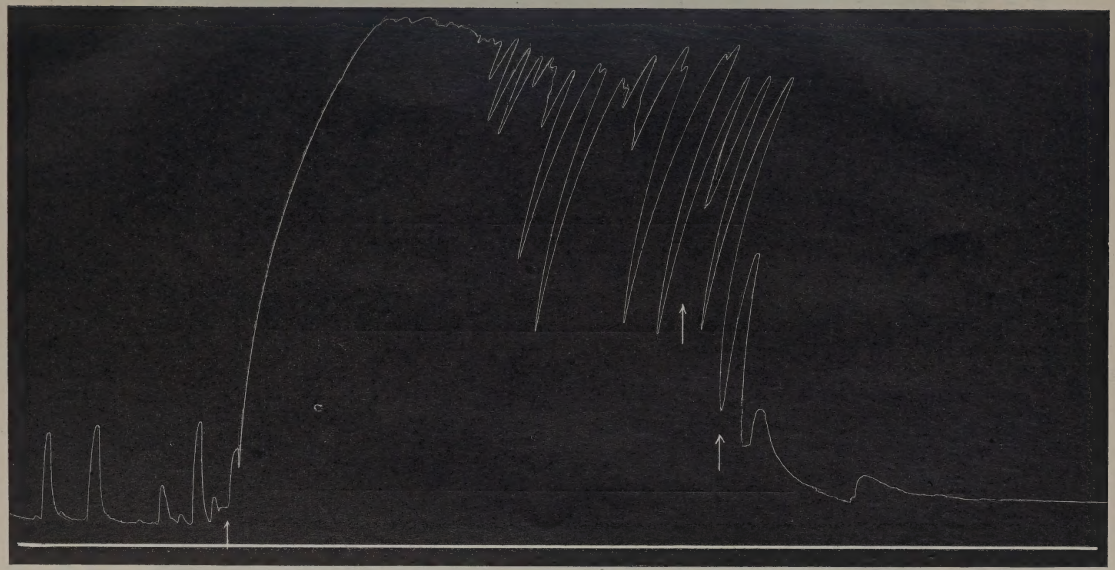

FIG. 1. Intestinal strip beating first in Ringer's solution. At x normal blood substituted; at y removed. At z blood from animal previously injected with 0.0037 gram nicotine was applied.

muscle was beating first in Ringer's solution. At x that solution was exchanged for blood A. The characteristic increase of tonus of the muscle, when freshly surrounded by blood, was at once recorded. At y blood A was removed, and at z blood B was substituted. The contractions were promptly inhibited, in a manner typical of the action of epinephrin. This observation was corroborated by other similar experiments, as shown in Table 1.

TABLE I

CAT	NICOTINE	SOLUTION	TIME OF EXTRACTING BLOOD B AFTER INJECTING NICOTINE	ACTION OF MUSCLE STRIP ON ADDITION OF BLOOD B
	grams	*cc.*	*minutes*	
1	0.025	5 (1 : 200)	5	Slight slowing of rhythm
			10	Contractions ceased (inhibition)
2	0.015	3 (1 : 200)	4	Inhibition
3	0.015	3 (1 : 200)	4	Slowing
			10	Further slowing and loss of tonus
4	0.0075	3 (1 : 400)	5	Slight loss of tonus and inhibition
5	0.004	1.6 (1 : 400)	3	Loss of tonus. Inhibition. Occasional contraction
6*	0.0037	0.75(1 : 200)	3	Loss of tonus. Inhibition
7	0.0037	1.5 (1 : 400)	1	Slight slowing
			8	Loss of tonus. Occasional contractions
8	0.0037	1.5 (1 : 400)	5	Loss of tonus. Inhibition. Occasional contractions
9	0.0027	1.1 (1 : 400)	3	Increased tonus. Contractions regular
				Dose subminimal ?

* Fig. 1.

Magnus has shown[7] that the action of nicotine (5 to 10 cg. added to 200 cc. of Ringer's solution) is to produce a brief inhibition of the rhythmic contractions of the isolated strip of intestinal muscle. Before the conclusion can definitely be drawn that epinephrin produces the inhibition obtained after injecting nico-

[7] Magnus: Arch. f. d. ges. Physiol., 1905, cviii, p. 17.

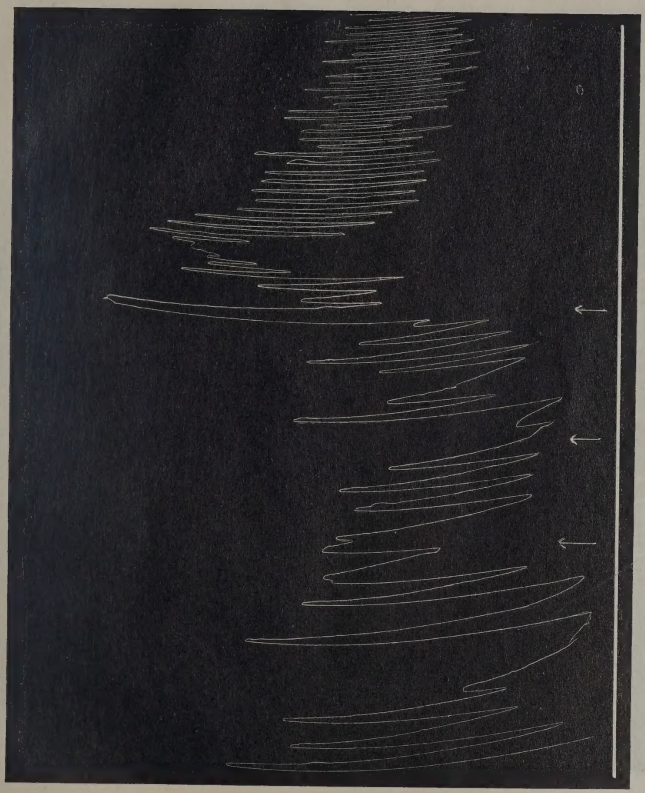

FIG. 2. Intestinal strip beating in about 3.5 cc. normal defibrinated blood. At x and y and z nicotine added—in all more than 1 cc. of 1:200 solution.

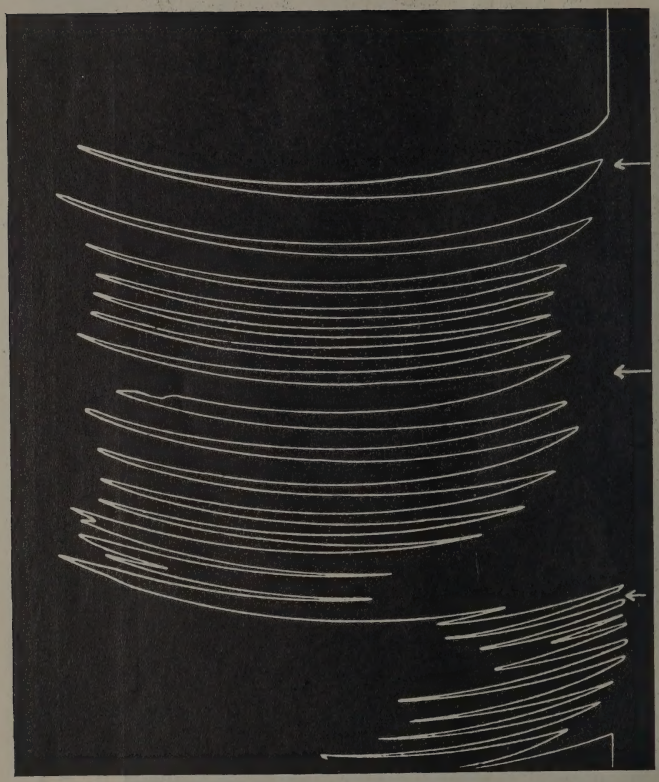

FIG. 3. Intestinal strip beating first in Ringer's solution. At *x* normal blood added, at *y* blood from decapsulated animal previously injected with 0.0075 gram nicotine was substituted. At *z* one drop of adrenalin (1:1000) was added.

tine, it is necessary to eliminate the possibility that the injected nicotine itself is the cause.

The effect of nicotine was tested by two methods. In the first, nicotine was added to the normal defibrinated blood in which the strip was contracting. In Fig. 2 is recorded the effects of small doses of nicotine on the contractions. At *x* and *y*, and *z*, nicotine was added, in all more than 1 cc. of a 1 : 200 solution. The amount of blood in the chamber was approximately 3.5 cc. When to this an amount of nicotine was added sufficient, if injected into a cat, to produce total inhibition of the contractions, there resulted not relaxation but increased tone and more rapid rhythm.

The second method of eliminating the possibility that injected nicotine caused inhibition of the pulsating strip was by testing the blood from decapsulated animals. Blood A was extracted as in previous experiments. The animals were then deprived of their adrenal capsules, and after twenty to thirty minutes they were given 0.0075 gram nicotine, a dose which, as Table 1 shows, is capable of producing complete relaxation of the test muscle. At the usual period after the nicotine injection blood B was extracted. In no case was there any loss of tone, slowing of the rhythm, or inhibition. In Fig. 3 these results are presented graphically. At *x* normal blood was added, at *y* blood taken from the animal after nicotine injection was substituted. The addition of one drop of adrenalin (1 : 1000) at *z* caused gradual loss of tone and inhibition, which proved that the muscle was still sensitive to the presence of epinephrin.

Nicotine, as used in these experiments, does not produce inhibition of the pulsating intestinal strip. Blood taken from near the openings of the adrenal veins after nicotine injection differs from blood removed from the same region before the injection, in producing inhibition of the pulsating strip. This difference does not appear if nicotine is injected after the adrenal glands have been removed. The conclusion is therefore justified that injection of nicotine in small amounts (0.0035 to 0.0075 gram in cats) results in augmented adrenal secretion.

WAVERLY PRESS, BALTIMORE